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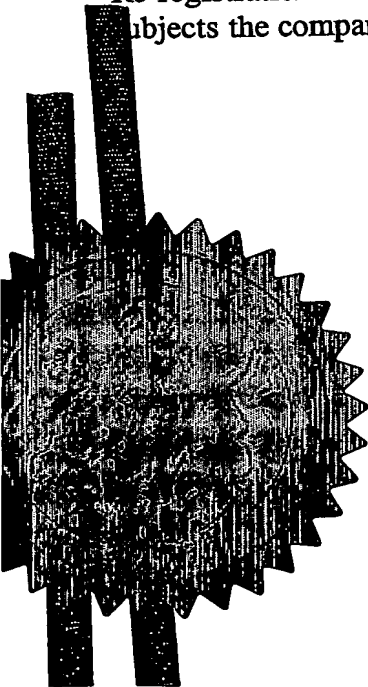
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FLUID ANALYSIS APPARATUS

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Philip Davies et al

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Fluid analysis apparatus

The present invention relates to a fluid analysis apparatus. More particularly, the invention relates to gas analysis apparatus that incorporates any one or more of a
5 pre-concentrator, a gas gating system and a single electron transistor detector.

A variety of techniques are known for the detection and analysis of gas phase analytes. The standard techniques presently used to detect low molecular concentrations typically involve mass spectrometry used in conjunction with pre-
10 concentration techniques and gas chromatography. In recent years, there has also been a drive to produce battery powered portable systems to enable in situ monitoring of, for example, industrial and volcanic emissions. However, such portable devices still weigh several kilograms and can have a somewhat limited sensitivity.

15

A number of so-called pre-concentrators are known that have been used to increase the sensitivity of gas analysis apparatus. The basic principle of a pre-concentrator is to collect molecules to be analysed (analytes) from a flow of gas. After a suitable collection period, the pre-concentrator is reconfigured (e.g. heated) such that the
20 collected analytes are released for subsequently analysis by an appropriate analyte detector.

An example of a pre-concentrator is described in US 6171378 and also by G. Frye-Mason *et. al.* in the paper 'Hand-Held Miniature Chemical Analysis System
25 (μ ChemLab®) for Detection of Trace Concentrations of Gas Phase Analytes', Micro Total Analysis Systems 2000, 229, 3 (2000). The pre-concentrator of G. Frye-Mason *et. al.* comprises a thin film layer of adsorbent material carried on a substrate and has the benefit of inherently low thermal mass and high thermal isolation. However, a significant drawback of the device is that the essentially planar adsorbent layer
30 means that large adsorbing areas require a large die area.

Another example of a pre-concentrator is described by Wei-Cheng Tian *et al.* in the paper entitled 'Microfabricated Preconcentrator-Focuser for a Microscale Gas Chromatograph', Journal of Microelectromechanical Systems, Vol. 12, No. 3, June 2003. This pre-concentrator comprises a plurality of channels defined, by deep reactive ion etching (DRIE), in high aspect ratio silicon. Commercially available adsorbent granules (e.g. Carbopack, Carboxen) of an appropriate particle size are located in the channels. Although such a structure provides an increased surface for a given substrate size, the flow of gas still passes over the bed, restricting its contact with the active surface of the adsorbent. Furthermore, the granules simply rest in the channels and are therefore not in intimate thermal contact with the heaters. The device of Wei-Cheng Tian *et al.* thus requires considerable power to heat the adsorbent granules and is quite slow to respond.

A number of gating systems are known for controlling the flow of gas through gas analysis apparatus. In particular, gas flow through a pre-concentrator must be controllably directed to either an exhaust port (e.g. when analytes are being collected by the pre-concentrator) or a detector (e.g. when the pre-concentrator releases adsorbed analytes). Typically, thermopneumatic valves based on diaphragm architectures have been used to provide the required gas flow control function.

Examples of thermopneumatic valves are described in Yang *et al.*, "A MEMS Thermopneumatic Silicone Membrane valve", Proceedings of IEEE The Tenth Annual International Workshop on Micro Electro Mechanical Systems (MEMS '97), Nagoya, Japan, January 26-30, 1997, pp. 114-118; Grosjean, C. *et al.* "A practical thermopneumatic valve", Micro Electro Mechanical Systems 1999 (MEMS '99), Twelfth IEEE International Conference, 17-21 Jan. 1999 Page(s): 147 -152); and J. S. Fitch *et al.* "Pressure-based mass-flow control using thermopneumatically-actuated microvalves.", Proceedings, Solid-State Sensor and Actuator Workshop, pp. 162-165 (Transducers Research Foundation, Cleveland, OH, 1998).

Disadvantages of prior art thermopneumatic valves include the requirement for active actuation to hold such gas control valves in one of their positions (e.g. power

must be continually applied to hold a normally open valve in the closed position). This leads to high power consumption, and thus a high energy budget. Furthermore, the flow of gas through such valves follows a convoluted route and the flow areas are restricted by the fundamental design of the device. Thermopneumatic valves also have a limited response speed and can suffer from hysteresis effects.

After the pre-concentration stage, analytes are released and carried through the gating stage to an appropriate detector. A number of miniature mass spectrometers are known; for example see J. Diaz *et al* "Sub-miniature double focusing sector field mass spectrometer for in situ volcanic gas monitoring", Am Soc. of Mass Spectrometry, Sanibel Island, FL, Jan 2000 and J. J. Tullistall, *et al* "Silicon micromachined mass filter for a low power, low cost quadrupole mass spectrometer", Proceedings of The Eleventh Annual International Workshop on Micro Electro Mechanical Systems, 1998 (MEMS '98), 25-29 January 1998, pp 438-442. Although such miniature mass spectrometers can provide the required analyte analysis, no system is known of truly sub-miniature proportions (e.g. having a volume less than 10cm^3). The generation of suitable vacuum conditions remains a major miniaturisation obstacle.

It is known that single-electron transistors (SETs) are presently one of the most sensitive detectors of electric charge available. SETs are capable of detecting an effective polarization charge, on or near the gate of the device, of the order of one thousandth of the fundamental electron charge. Chemical sensing using such SETs has thus been proposed previously. However, the majority of previous work on single electron behaviour has been confined to very low temperatures (4.2K or less) in devices fabricated from gated semiconductor microstructures; for example see L.P. Kouwenhoven *et al*, Proceedings of the NATO Advanced Study Institute on Mesoscopic Electron Transport, edited by L.L. Sohn, L.P. Kouwenhoven, and G. Schön (Kluwer Series E345, 1997) p. 105-214.

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Recently, a number of experiments have shown single-electron effects at room temperature, in which the confining region is very small. For example, see Y.

Wakayama et al., J. Appl. Phys. 94, p.4711 (2003) and W. Liang et al, Nature 417, p.725 (2002). These experiments use gold nano-particles and single molecules, including C60. Although these experiments highlight the potential for room temperature SET operation, they are impractical for use in gas sensors due to the difficulty in making reliable and reproducible contacts; for example, methods such as break junctions and scanning tunnelling microscopy (STM) tips are employed.

Accordingly, it is an object of the present invention to provide a compact fluidic analyser that mitigates at least some of the above mentioned disadvantages of known analyser systems. It is a further object of the invention to provide a pre-concentrator that mitigates at least some of the above mentioned disadvantages of known pre-concentrators. It is a further object of the invention to provide a gas gating device that mitigates at least some of the above mentioned disadvantages of known gas valve arrangements. It is a further object of the invention to provide a single electron transistor detector that mitigates at least some of the disadvantages of known SET based detectors.

According to a first aspect of the invention, a fluidic analyser comprises a pre-concentrator, a fluid gating device and a detector, the fluid gating device being arranged to selectively route fluid from the pre-concentrator to either one of the detector and an exhaust port, characterised in that the pre-concentrator, fluid gating device and detector are each formed as substantially planar layers and arranged in a stack.

The present invention thus provides a fluidic analyser in the form of a compact hybrid stack or "cube". For example, a three layer vertical stack may be provided that comprises a fluid gating device layer that is sandwiched between the pre-concentrator layer and the detector layer. In use, an acquisition mode is first employed in which a fluid is passed through the pre-concentrator and directed, via the fluid gating device, to an exhaust port. In acquisition mode, the pre-concentrator is arranged to adsorb analytes. After a predetermined period, the device is switched into detection mode. In detection mode, the pre-concentrator releases the captured

analytes (e.g. by heating the adsorbent material) which are directed, via the fluid gating device, to the detector for analysis.

5 Providing each analyser function (i.e. pre-concentration, fluid gating and detection) in a planar layer enables the device volume to be greatly reduced compared with prior art devices of the type described above. Furthermore, the flow path between each layer is significantly smaller than the flow path between the adjacent components of a prior art device thereby enhancing device sensitivity.

10 Advantageously, the pre-concentrator comprises a layer of material having a plurality of apertures through which fluid can be passed, the internal surfaces of said apertures being adapted to releaseably retain (e.g. reversibly adsorb) analytes from a fluid. A compact, highly efficient, pre-concentrator is thus provided. More details of the preferred features and various advantages of a pre-concentrator of this type are
15 described below in relation to the second aspect of the invention.

Conveniently, the fluid gating device comprises a first outlet and a moveable member, the moveable member providing control over the flow of a received fluid to the first outlet, wherein the device is formed from a substantially planar substrate
20 and in that the moveable member comprises a shutter that is moveable in the plane of the substrate. A compact planar fluid gating device is thus provided. More details of the preferred features and the various advantages of a fluid gating device of this type are described below in relation to the third aspect of the invention.

25 Preferably, the detector comprises a single electron transistor (SET) having a quantum dot region, wherein at least one molecule is attached to the SET in the vicinity of the quantum dot region and in that a receptor site for analytes is additionally provided adjacent said at least one molecule. A high sensitivity, compact detector is thus provided. More details of the preferred features and the
30 various advantages of a single electron transistor based detector of this type are described below in relation to the fourth aspect of the invention.

Advantageously, the fluidic analyser further comprises a pump to drive the fluid through the pre-concentrator and fluid gating device. The pump may have a variable power such that the fluid pressure can be increased or decreased as required. For example, a higher pressure may be required when the analyser is operating in acquisition mode compared with detection mode. Also, it may be advantageous to reduce fluid pressure (and hence the force against which any shutter or valve arrangement must operate) when the fluid gating device is switching fluid flow from the detector to the exhaust port or vice versa.

10 Conveniently, a power source is also provided. For example, batteries or other power cells.

According to a second aspect of the invention a pre-concentrator is provided for releaseably retaining analytes from a fluid, characterised in that the pre-concentrator comprises a layer of material having a plurality of apertures through which fluid can be passed, the internal surfaces of said apertures being adapted to releaseably retain analytes from a fluid.

The pre-concentrator of the present invention thus comprises a layer of material (e.g. a silicon wafer) in which a plurality of apertures are formed to produce, for example, a honeycomb type structure. The internal surfaces of the material forming the apertures are adapted (e.g. by applying a coating or surface treatment) to releaseably retain (e.g. reversibly adsorb) molecules from a fluid. Passing a fluid through the apertures of such a honeycomb structure, rather than over a pre-concentrator layer as described in US6171378, enables a much greater surface area to be placed into contact with the analyte carrying fluid. A more compact pre-concentrator can thus be provided.

Conveniently, the internal surfaces defining the apertures are porosified to enhance the effective surface area of the pre-concentrator. Alternatively, or additionally, the surface area of the pre-concentrator is enhanced by the direct application of a high capacity trapping matrix in thin film form (e.g. porous silicon films via sol gel

processing and direct application of thin film polydimethylsiloxane, or PDMS). In the case of silicon, it has been found that the formation of a porous layer can increase the effective surface area by up to a factor of one hundred as compared with an untreated planar silicon wafer; this improvement multiplies with the factor of ten
5 improvement available through the creation of a vertical honeycomb structure giving an overall adsorption enhancement factor of up to about one thousand.

Advantageously, the substrate comprises a layer of silicon, said apertures being formed through said layer of silicon. Silicon is preferred due to the ease of
10 manufacture and the ability to readily porosify the material. In addition, a variety of techniques are well known in the art for modifying the surface chemistry of silicon and its oxides by the addition of organic functional groups. Alternative materials may also be used as the be used for the layer of material such as silicon dioxide, glass or polymers/plastics.

15 Conveniently, the apertures are formed in the layer of material by deep reactive ion etching (DRIE). DRIE offers a convenient means for producing apertures in wafers of semiconductor material, such as silicon. For example, DRIE may be used to provide narrow apertures having a 30µm diameter and a length of several hundred
20 microns; such apertures ensure an efficient interaction of the fluid with the concentrator surface. Aperture sizes of 5-100µm diameter and 50-1000µm length may be readily produced using such technology.

Conveniently, the layer of material comprises a regular array of apertures which may
25 advantageously be arranged to form a honeycomb structure.

Preferably, the internal surfaces of the apertures are coated with adsorptive material. Alternatively, the surface of the apertures may be altered to provide the required adsorption properties. A multitude of surface chemistries can be generated to
30 provide the required structure by, for example, vapour deposition of suitable materials, or the addition of suitable organic functional groups to the surface by standard techniques. For example, short chain polysiloxane molecules may be

grafted onto the surface which, being hydrophobic, will reject water and offer some selective adsorption.

Furthermore, said layer of material may additionally comprise a heater element. The
5 heater element may be formed by forming a conductive region (e.g. by doping a semi-conductor) in the layer. The provision of integrated heaters will allow rapid heating of the internal surfaces of the apertures to release captured analyte. Alternatively, conductive tracks (e.g. metallic lines) may be formed on or in the layer. Discrete heater elements may also be attached to the layer. A heat sensor (e.g.
10 a platinum track) may also be incorporated in to the layer of material so that the temperature of the first layer of material may be monitored.

The heated layer of material is preferably isolated from subsequent device layers and the package by including a thermal isolation layer (e.g. a glass interface) between
15 the pre-concentrator and the underlying substrate (e.g. a gas gating chip). The low thermal conductance of such a material arrangement enables the achievement of fast response times.

According to a third aspect of the invention a fluidic device comprises a first outlet
20 and a moveable member, the moveable member providing control over the flow of a received fluid to the first outlet, characterised in that the device is formed from a substantially planar substrate and in that the moveable member comprises a shutter that is moveable in the plane of the substrate.

25 A fluidic device is thus provided having a moveable shutter that provides control over the flow of a received fluid to a first outlet (e.g. an outlet that is coupled to a detector). In other words, in-plane movement of a shutter is used to constrict the flow path to a first outlet by, for example, covering the entrance aperture of the outlet. The provision of a shutter that moves in the plane of the substrate overcomes
30 several disadvantages of the thermopneumatic devices of the prior art. For example, a MEMS type shutter can be more rapidly moved between the open and closed positions without suffering the temperature hysteresis effects reported in the

literature for thermopneumatic valves. Furthermore, a MEMS shutter and associated actuation mechanisms can be formed from a single layer of a substrate (e.g. on a silicon wafer). Such an arrangement can be much smaller than the various prior art valves described above. As described below, the shutter device may be held open or closed, or in any one of a plurality of intermediate positions to provide the required flow control. Furthermore, clamps or latches may be provided to hold the shutter in the open, closed or intermediate positions.

Advantageously, the device further comprises an exhaust outlet for receiving any fluid that is prevented, by said moveable member, from passing to said first outlet. The device can thus be arranged to selectively pass fluid to the first outlet (e.g. for onward passage to a detector) or to an exhaust outlet. As described below, this arrangement is particularly suited to fluid analysis apparatus in which gas from a pre-concentrator is directed to a detector only when analytes are released therefrom (i.e. in detection mode).

Conveniently, fluid is received by the device from a direction substantially perpendicular to the plane of the substrate and/or the first outlet is defined in the planar substrate as a channel having an axis substantially perpendicular to the plane of the substrate. Fluid entering the device (e.g. through an input aperture) will thus impinge on the shutter from an orthogonal direction. Similarly, fluid that exits the device via the first outlet will pass along the same direction. In such a configuration, the shutter is not required to move against the force of the incident fluid when being moved in to, or out of, the fluid path. A smaller force can therefore be used by the actuation means associated with the shutter when moving between the open and closed positions. It would be appreciated that, in certain configurations, the fluid pressure may force the shutter into contact with the substrate from which it is suspended. In such a case, it may be necessary to reduce the fluid pressure when moving the shutter.

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The shutter may advantageously be shaped such that it can engage and seal the entrance to the channel defining the first outlet. In this manner, the pressure of

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incident fluid on the shutter can actually be used to improve the seal. For example, a circular shutter may be provided in conjunction with a correspondingly circular entrance to the first outlet. In use, the shutter may be moved into the closed position and hence cover the first outlet. Any applied fluid pressure may then force the shutter to tightly engage and seal the outlet. Furthermore, a raised annular sealing ring portion may also be provided around the circumference of the first outlet. Engagement of the shutter with such a sealing ring can further improve the quality of the fluid seal.

10 Conveniently, the shutter can adopt either one of an open position and a closed position, the open position allowing fluid to pass to the first outlet and the closed position preventing fluid from passing to the first outlet. It is also preferred that, when the shutter is in the closed position, any received fluid is directed to an exhaust port.

15

Furthermore, when the shutter is in the open position, fluid may be advantageously prevented from flowing to the exhaust port. For example, the shutter, or another portion of the moveable member, may be arranged to block the exhaust port when the shutter of the device is in the open position.

20

Conveniently the moveable member comprises means for retaining the shutter, without the application of power, in the open position or the closed position as required. For example, a latching and/or clamping mechanism may be provided. The means for retaining the shutter may also retain the shutter in an intermediate position if required. This is a significant advantage over the prior art thermo-pneumatic valves described above which required the continual application of power to remain in one of the their states.

25 Conveniently, the fluidic pathway through the device when the shutter is in the open position is minimised. This reduces the possibility of analytes contained in a gas phase from becoming attached to portions of the gas gating device. Furthermore, it is advantageous for the dead space of the device (i.e. space within the device into

which fluid can flow but not comprising part of the flow path) when in the open position to be minimised. Again, this prevents loss of analytes. A skilled person would appreciate that sealing arms could be provided to perform such a function.

5 Advantageously, the shutter is a micro-electromechanical (MEMS) shutter. Conveniently, the moveable member comprises a MEMS electro-thermal actuation mechanism to impart movement to the MEMS shutter. Furthermore, it is preferred for the moveable member to comprise a MEMS compliant displacement mechanism; the amplitude of movement produced by the actuation mechanism can then be
10 amplified to increase the amount of shutter travel that can be obtained. Herein, MEMS is taken to include micro-machined elements, micro-systems technology, micro-robotics and micro-engineering and the like.

Conveniently the planar substrate comprises silicon. For example, a silicon-on-
15 insulator (SOI) wafer or the like may be used. Advantageously, the device is fabricated using a deep reactive ion etching (DRIE) process.

Although the invention can operate on any fluid (e.g. liquid or gas), it is preferable to apply the device to gas based application and a gas flow controller may thus be
20 provided. If a liquid is employed, the skilled person would appreciate the various sealing techniques that could be used to prevent the liquid from adversely affecting the operation of the device (e.g. by heat transport from electro-thermal actuation mechanisms etc) of the device.

25 According to a fourth aspect of the invention a molecular detector is provided that comprises a single electron transistor (SET) having a quantum dot region, characterised in that at least one molecule is attached to the SET in the vicinity of the quantum dot region and in that a receptor site for analytes is additionally provided adjacent said at least one molecule.

30

A molecular single electron transistor (MSET) is thus provided that has the ability to detect single molecules of interest. The device operates by locating at least one

molecule in the quantum dot region of a SET. Analysis of the SET properties (e.g. conductance as a function of gate and source-drain voltage) provides a characteristic response that depends on the electrical properties of the attached molecule. Any change in molecular electrical characteristic results in a change in the electrical properties of the SET. When a molecule binds to the receptor site that is provided in the vicinity of the at least one molecule, a measurable alteration of SET electrical properties will thus occur. The receptor site for analytes may form part of the at least one molecule or it may be separate and located near the at least one molecule. A detailed analysis of SET electrical properties can also be used to determine certain properties of the analyte (e.g. to distinguish different types of analyte).

A molecular SET (MSET) of the present invention thus has several advantages over prior art SETs from the chemical sensing point of view. For example, the device is capable of being operated at room temperature thus removing the requirement for cryogenic cooling systems. Furthermore, the room temperature operation does not rely on esoteric methods such as the injection of charge into a gold nanoparticle via an STM tip. In addition, the high sensitivity provides comparable results to mass spectrometer systems which are inherently physically larger than MSET devices.

As described in more detail below, the molecule attached to the SET is ideally a conjugated organic rod. Preferably, the molecule also comprises a side group that can provide the receptor site. In other words, the organic molecule features specific functional groups (receptors), which bind the molecule of interest and give observable conductance changes.

Alternatively, or additionally, a receptor may be located near (i.e. in the vicinity of) the at least one molecule; for example, it may be located on the substrate of the single electron transistor in the vicinity of the at least one molecule. The presence of a molecule at such a receptor site will induce a detectable change in the electrical properties of the attached molecule.

Advantageously, a first end of the at least one molecule is attached to the source electrode of the single electron transistor and a second end of the at least one molecule is attached to the drain electrode of the single electron transistor. Conveniently, the first and second ends of the at least one molecule are attached to
5 the source and drain electrodes respectively via tunnel barriers.

Conveniently, a self-assembled monolayer of molecules is located between the source and drain electrodes of the single electron transistor.

10 Preferably, the device additionally comprises means for measuring SET conductivity as a function of gate voltage. Furthermore, the device may advantageously comprise means for measuring SET conductivity as a function of source-drain voltage. A conductivity map as a function of gate voltage and source-drain voltage can thus be produced. The characteristics of such a map highlight so-called "quantization gaps"
15 in the energy spectrum, these not only enhance the Coulomb blockade effect but also give rise to resonances in conduction that depend on the properties of the attached molecule. This allows molecular identification of the analyte.

The single electron transistor of the present invention can advantageously be formed
20 using a complementary metal oxide semiconductor (CMOS) process; for example a standard 0.35 μ m CMOS process. Such a process provides a suitable geometry for a molecular SET in the form of the gate oxide gap. Electrical contact with the at least one molecule can be made by using heavily doped Silicon contacts. The spacing between the source-drain contacts (i.e. the gap where the at least one molecule is
25 attached) may be controlled down to monolayer accuracy. Once fabricated, the at least one molecule can be subsequently attached.

A MSET can thus be formed using standard CMOS techniques. In the same process, any associated control and/or amplification circuitry may be fabricated. A single
30 chip can thus be provided that comprises an integrated detection device with on-chip processing of the picoamp scale currents of the MSET. This will ensure good reproducibility in the fabrication process as compared with the hand-crafted

processes using, for example, the deposition of gold nanoparticles. When combined with molecular self-assembly processes it should be possible to produce arrays of MSETs with identical characteristics offering, for example, built-in redundancy.

- 5 A CMOS based single electron transistor may also be provided having source and drain electrodes held in spaced relation, said source and drain electrodes being adapted such that each end of a rod shaped molecule may be attached thereto. Attachment of an appropriate molecule to such a structure allows a MSET detector of the type described above to be provided.

10

In accordance with a fifth aspect of the invention a fluid analyser is provided that incorporates a pre-concentrator according to the second aspect of the invention, and/or a fluidic device according to the third aspect of the invention and/or a detector according to the fourth aspect of the invention.

15

The invention will now be described, by way of example only, with reference to the following drawings in which;

Figure 1 shows a schematic view of a gas analyser of the present invention,

20

Figure 2 shows the pre-concentrator of the gas analyser system,

Figure 3 shows a cross-sectional view of vias etched in a silicon wafer,

- 25 Figure 4 shows a TEM image of highly porous silicon,

Figure 5 shows the modelled temperature distribution of the pre-concentrator of figure 2,

- 30 Figure 6 shows the gas shutter of the gas detection system in an open (figure 6a) and closed (figure 6b) configuration,

Figure 7 shows an example of a gas shutter of the type described with reference to figure 6.

Figure 8 is a schematic illustration of the molecular single electron transistor (MSET) detection device of the gas detection system.

Figure 9 shows a schematic diagram of the receptor portion of the MSET (figure 9a) and a band structure representation of the device (figure 9b).

Figure 10 illustrates the 2D conductance maps for a conventional SET (figure 10a) and a MSET (figure 10b), and

Figure 11 shows a molecule "T" that can form the basis of the molecule used in the MSET of figures 8 to 10.

15

Referring to figure 1, a gas analyser 2 of the present invention is shown. The analyser 2 is formed as multi-layer hybrid structure, or MEMS cube, and comprises a pre-concentrator layer 4, a gating layer 6 and a detector layer 8.

20 The pre-concentrator 4 consists of a honeycombed silicon wafer and performs the function of pre-concentrating. The internal surfaces of the through-wafer vias of the honeycomb layer are coated with a trapping layer for molecules of interest and the low thermal mass structure is heated by integral resistive heater elements. The gating layer 6 comprises an electro-thermally operated MEMS shutter 10 that allows gas to
25 be directed to either an exhaust port 12 or to the detector layer 8.

The detector layer 8 comprises a Molecular Single Electron Transistor (MSET) detector 14 integrated onto a silicon-ASIC chip. The MSET detector comprises a conjugated organic rod to form the quantum dot region. This is joined to silicon
30 electrodes via tunnel barriers thereby giving rise to quantum confinement in the dot region. In a detection event, the molecule of interest will bind to an appropriate receptor attached to the organic quantum dot. The binding of just a single molecule

to a receptor should give rise to measurable changes in the conductance properties of the device at room temperature.

5 In use, the apparatus initially adopts the molecule collection arrangement shown in figure 1a. In this configuration, the gas of interest is passed through the pre-concentrator 4 and directed out of the exhaust port 12. Any molecules of interest will bind to the trapping layer of the pre-concentrator 4.

10 After a certain sampling period, the MEMS shutter 10 is moved such that the analyser adopts the arrangement shown in figure 1b. The heaters of the pre-concentrator 4 are then used to heat the trapping layer and any molecules of interest are released therefrom. These released molecules are then directed, via the gating layer 6, to the detector layer 8 where they can be detected by the MSET detector 14.

15 It should be noted that each of the individual layers forming the stack will require alignment with respect to one another. The pre-concentrator and gas gating chips can utilize conventional bonding techniques, as these chips will be tolerant to thermal treatments. The detector chip, containing (thermally sensitive) electronics and the MSET are bonded using a low temperature polymer-based bonding technique. It is
20 estimated that an the integrated system's energy consumption per layer per measurement will be: less than 100mJ for the pre-concentration, less than 100mJ for the gas gating structure and less than 350mJ for the detection circuitry. Thus, the estimated total energy per measurement is less than 1J excluding the energy required to flow the sample through the device.

25

The analyser of the present invention offers a number of advantages over prior art systems. For example, the analyser could be fabricated to be around 2cm^3 in size and is thus considerably smaller than prior art devices. However, despite the smaller
30 size, the device can offer up to a one hundred-fold increase in sensitivity for the detection of certain molecular species as compared with known mass spectrometer systems. The inherent design of the cube can also reduce vapor dead space and should enhance detector sensitivity for more reliable detection with fewer false readings. In addition, the MEMS components are highly mechanically robust.

Detailed descriptions of the various layers forming the gas analyser are provided below. Although the combination of the described pre-concentrator, gating structure and MSET provide an analyser with the advantages described above, the skilled person would recognise that any one or more of these components may advantageously be used in a gas analysis system.

The Pre-concentrator

10 Referring to figure 2, a pre-concentrator 20 of the present invention is shown. The pre-concentrator comprises a honeycomb region 22 supported on a glass carrier 24. For a gas analyser of the type described above, the honeycomb region is typically 0.5mm square. However, the skilled person would appreciate that the size and/or shape of the region 22 can be chosen as required for the particular application.

15

The honeycomb region 22 is fabricated from high aspect ratio silicon, patterned using DRIE (deep reactive ion etching). This process technology allows a rugged honeycomb type structure to be realised with a low thermal mass, several square millimetres surface area and good flow characteristics. Holes having a pitch of 20 40µm and a diameter of 20µm can be readily formed using such a technique; figure 3 is a photomicrograph of such holes (or vias) 32 formed in a silicon wafer 30. The inner surface of the vias 32 may also be porosified using, for example, stain etching or anodisation to further enhance the surface area in contact with the sample vapor. Figure 4 shows an example of such a high surface area porosified material. 25 Porosification will increase the surface area by a factor of around one hundred and can also allow a suitable adsorbing surface chemistry to be created at the surface.

The holes 32 may be lined with a variety of appropriate chemical layers or a given surface treatment (e.g. self-assembled monolayers) may be applied. The various 30 linings or treatments that may be applied to the holes, for example a stable hydrophobic or hydrophilic coating, may be arranged to selectively trap only certain

molecule(s) of interest. The person skilled in the art would be aware of the various layers/treatments that can be used to trap molecules for various applications.

- In the device shown in figure 2, conductive p-type silicon is used to form the honeycomb region 22. This allows the silicon structure of the honeycomb to form a resistive heater thereby removing the requirement for metal heater tracks. This arrangement also provides accurate temperature control thereby increasing desorption selectivity. Polysilicon or platinum layers may alternatively or additionally be included in the structure to form a resistive heater or integrated temperature sensors; these layers may be formed on the top surface of the wafer and/or integrated into the vertical holes. It should be noted that the honeycomb structure may be formed in a variety of alternative materials; for example other semi-conductor materials, or in micro-moulded plastic.
- Although by no means essential, the honeycomb region 22 may be mounted on a glass carrier 24. The glass carrier 24 may be patterned (e.g. with trenches 26) to both limit the thermal heat loss from the pre-concentrator and to allow fluidic communication through the plane of the device to any substrates below. The high thermal conductivity of the silicon, relative to the glass carrier, helps ensure that the uniformity of heating is high across the active area of the pre-concentrator. The exact structure of the pre-concentrator can, of course, be optimised for best thermal performance for a given application.
- Figure 5 shows the predicted thermal properties of a pre-concentrator structure of the type shown in figure 2. Table 1 also outlines the thermal properties of a pre-concentrator of the type described above.

Parameter	Value
Silicon thickness	150 μm
Hole pitch	50 μm
Hole size	30 μm
Silicon volume	0.054mm ³
Glass thickness	500 μm
Bond contact area	0.271mm ²
Honeycomb footprint	0.25mm ²
Active adsorbing area (neglecting effects of porosification)	2.1mm ²
Thermal time constant	120ms
Input power	250mW
Time to rise 200K	110ms
Energy consumption	0.03J

Table 1: Parameters and modelled performance for a 0.5mm by 0.5mm pre-concentrator honeycomb

- 5 The thickness and footprint of the pre-concentrator structure may be readily tuned to achieve an appropriate compromise between power budget, thermal response time and active area. For example, increasing the honeycomb footprint to 1mm² yields an absorber area (untreated) of around 10mm². Increasing the power applied to 0.5W leads to a 200K rise time of around 120ms, and an energy requirement of around
- 10 0.06J

It can thus be seen that the vertical architecture of the pre-concentrator of the present invention enables compact and practical integration, with the minimum dead volume, within a gas analyser device.

15

Gas gating structure

As described above with reference to figure 1, the gas gating structure is arranged to include a physical valve that enables gas to be directed along either one of two

different routes. The first route permits a rapid gas flow through the device avoiding the gas detector and the second route allows gas flow to be diverted onto the detector chip. The second route is selected to coincide with the controlled release of the pre-concentrated agents from the pre-concentrator.

5

Referring to figure 6, a gas gating arrangement incorporating a substrate port 64, an exhaust port 66 and moveable MEMS shutter 60 is shown. The MEMS shutter 60 is supported on an armature 62. The armature is attached to a compliant displacement multiplier (not shown) which is in turn attached to a bent beam electrothermal actuator (not shown). The bent beam actuator applies a displacement to the compliant structure which displaces and rotates the armature 62. This allows the shutter 60 to move between the first position of figure 6a and the second position of figure 6b.

10

15 Gas from the pre-concentrator is incident on the gas gating arrangement in a direction perpendicular to the plane of the surface and along an axis co-incident with the axis of the substrate port 64. In the first position shown in figure 6a, the substrate port 64 is closed and gas passes along a first route and exits the gas gating arrangement via the exhaust port 66. In the second position shown in figure 6b, the exhaust port 66 is closed and gas passes along a second route and exits the gas gating arrangement via the substrate port 64.

20

A sealing arm 68, and a corresponding recess 70 in the substrate, are also provided. The sealing arm is arranged such that, when the shutter is in the second position of figure 6b, the amount of "dead-space" within the flow path is minimised by blocking gas flow into the hollow regions of the substrate in which the MEMS armature and actuator are formed. This ensures the maximum number of molecules of interest are passed to the detector.

25

30 The gas-gating structure is fabricated using deep reactive ion etching (DRIE) of 'through-wafer' silicon channels, and a DRIE step is used to form the micro-machined MEMS silicon shutter (valve) system on an SOI substrate.

The MEMS shutter arrangement shown in figure 6 can be readily provided with around 0.5mm throw actuation. The MEMS shutter 60 can also be opened and closed within a few milliseconds thereby ensuring that gas flowing from the pre-concentrator to the sensor contains the maximum number of molecules of interest and the minimum amount of interferents. In the open position, the released molecules of interest will have line of sight access to the sensor; this is in contrast to the tortuous path through the prior art MEMS based valves that are described above.

10 The MEMS shutter arrangement of the present invention also has a power consumption of less than a watt. Furthermore, the use of an electro-thermal hold latch to fix the shutter in the open position when required minimises the average power consumption, and makes the device a suitable candidate for use in a system with a low energy budget. The energy required to open and latch the shutter is
15 around 0.05J, and zero power is required to hold the shutter in position. The voltage of operation can be tuned by selection of the dopant concentration in the material forming the electrothermal actuator.

The use of the MEMS shutter arrangement in a fluidic system enables a very large
20 flow area. This enables higher rates of fluid flow in both open and closed positions compared with prior art diaphragm valve systems. When the shutter is in the closed position (i.e. gas directed to the exhaust port), the air may be routed around the shutter through a recess above the shuttered area. Air flowing onto the shutter will tend to force it closed, and maintain a seal. When the shutter is in the open position
25 (i.e. gas directed to the substrate port), the shutter blocks the path through the recess, and air is routed through the substrate port, directly onto the detector below. Again the action of the air pressure will help to seal the shutter. During switching between the open and closed states, the gas flow may be reduced to reduce the pressure on the shutter element.

30

Referring to figure 7, examples of a shutter design in the open (figure 7b) and closed (figure 7a) positions is given. Figure 7b is a photomicrograph of an SOI based device under actuation.

The MSET detector

Referring to figure 8, a schematic of a molecular single electron transistor (MSET) structure of the present invention, fabricated using CMOS device processing, is shown. The MSET comprises a silicon source electrode 82, a polysilicon drain electrode 84 and a polysilicon gate electrode 86. An active region 88 (shown in more detail in the figure 8 inset) comprises a self-assembled monolayer of organic molecules lying between the source and drain electrodes.

10 The organic molecules 87 of active region 88 comprise a conjugated organic rod (the quantum dot region) which is joined to silicon electrodes via tunnel barriers. This gives rise to quantum confinement in the dot region as described in more detail below. In operation, with a small source-drain bias, the gate is biased such that the single electron current from source to drain is at the steepest part or the
15 transconductance curve.

A first binding site 90 is provided on the organic molecule 87 and/or a second site 92 is provided on the substrate. The presence of a single molecule of interest binding at the first site 90 or the second site 92 will lead to an observable change in source-
20 drain current and hence detection. Further discrimination of the adsorbed molecule(s) is possible by analyzing I-V 'signatures', as discussed in more detail below, when both the source-drain and the gate biases are varied.

Referring now to figure 9a, a schematic representation of the active region of an
25 MSET device of the invention is shown in more detail. The MSET structure can be conceptualised as a molecular semi-conducting core 100 located between two electronically insulating σ -bonded groups 102. A chemically active group 104 attached to this core will bind molecules of interest. Each end of the molecule 100 will be chemically bound to the silicon electrodes 106. Figure 9b shows a band
30 structure representation of the device shown in figure 9a in which ΔV represents the effect on the molecular states of small electrostatic perturbations (e.g. a docked molecule).

Conductivity through the MSET is controlled by both gate voltage (V_g) and source-drain voltage (V_{DS}). The resultant conductivity map as a function of V_g and V_{DS} is shown schematically in figure 10a. In figure 10a the differential conductance is shown in grey scale with the centre of the 'cross' at zero (or small) source-drain bias corresponding to a gate voltage for which the first LUMO (lowest unoccupied molecular orbit) levels come into resonance, including the effect of Coulomb charging energy.

Figure 10a represents what this would be like with just coulomb blockade (eg conventional SET), whereas the MSET device would show additional structure specific to the electronic properties of the molecule used as shown in figure 10b. This signature would be very sensitive to the details of the docked molecule and could be used to identify the adsorbed molecule. The molecular identification process can be aided using quantum mechanical calculation of the energy levels for the molecular backbone alone, and also for the backbone with the analyte (i.e. molecule of interest) attached. These energy levels can then be used to enhance orthodox theories of SET transport to predict I-V characteristics and conductance maps for MSETs. This enables unique identification of docked molecules, and will also guide the design and synthesis of backbone and receptor molecules.

A low noise amplifier is required to detect the small (pico-Amp) current displacements related to the detection events. Such an amplifier can be fabricated on a foundry 0.35 μ m CMOS process. The detector circuit can be fabricated using the same CMOS (0.35 μ m) process technology that is used to produce the MSET. The MSET and amplifying circuitry can thus be fabricated in the same process flow and hence on the same silicon chip. In order to complete the fully integrated MSET device, post-processing will be required to open access windows in the CMOS passivation layers to the MSET support structure followed by introduction of the relevant organic molecules in the form of a self assembled monolayer. Differential measurements and provision of an array of detectors on a single chip is also possible.

The attachment of the active molecule to the silicon electrodes is accomplished by chemical bonding. The molecule is preferably attached at each end, so a di-functional, symmetric molecule is preferred. Various attachment options would be
5 apparent to a person skilled in the art, for example:

(i) Oxidation of the silicon surface to silicon dioxide will provide a surface suitable for docking with trialkoxy silane groups. This chemistry is well established and allows the formation of dense self-assembled monolayers of molecules. It is
10 straightforward to apply this technique to fabricate sparse arrays of active molecules for SETs.

(ii) Chlorination of the silicon surface provides an array of active Si-Cl bonds which can be reacted with organic amines to provide a tightly bound layer.
15 Assembly of dense layers of aliphatic and aromatic amines can be achieved, and the method has the advantage that the organic amines are relatively easy synthesis targets.

(iii) Reaction of a silicon surface with an organolithium reagent or Grignard
20 reagent provides a route to surface bound organic molecules. The reaction can be facilitated by chlorination of the surface, or electrochemically.

(iv) Organic alkenes can be bound to silicon having Si-H surface groups by a hydrosilylation reaction.
25

The above options encompass a wide range of organic materials and surface treatment conditions; the choice of which to use will be determined by ease of synthesis of the molecule and compatibility of the process with all the materials and the various structures present.

30 The molecule attached to the SET is preferably a rod-shaped molecular wire of length sufficient to bridge the CMOS gate oxide thickness. The molecule shown in figure 11, hereafter referred to as molecule "T", represents a molecule that can form the basis of the molecule that is used. This molecule (I) has already been synthesised

25

in excellent purity and high yield for docking onto gold electrodes. The length of the molecule is 6.8nm. Lateral substituent groups are provided to maintain its solubility, but are omitted for clarity. Molecule (I) has an appropriate molecular length, reversible electrochemical doping (reduction) even in solution, and functional groups at each end for attachment to a surface. Further work has demonstrated that functional groups can be attached laterally to (I) to provide a receptor site for chemical sensing.

Various changes are required to molecule I to make it suitable for use in a SET. Firstly, the molecular rod is modified to provide electronically insulating units at each end; alicyclic units such as 2,2,2-bicyclooctane provide candidate units which maintain the rigidity of the structure. The end groups are also altered to make them suitable to bind to silicon, rather than gold. Chemical receptor units tailored to selectively bind the molecules of interest are incorporated; strongly basic groups which will bind to molecules by displacement of F or alkoxy units are preferred. The molecular length is also tailored to match the gate oxide thickness accurately; this facilitates docking on the electrodes in a unique environment. It is well known that molecular length can be controlled at the synthesis stage in increments of 0.2-0.3nm by adding atoms, and on a finer scale by exchange of chemical groups for ones having slightly longer or shorter bond lengths.

By adding a receptor incorporating a nucleophilic group, the MSET will bind fluorophosphonate agents, e.g. pesticides, by nucleophilic displacement of F. Further discrimination can be provided by having an array of MSET detectors with different receptors attached to the backbone molecules.

During fabrication of the MSET, photoelectron spectroscopy can be used to provide a sufficiently sensitive probe to monitor deposition of the organic material on the electrode surfaces, and allow the degree of coverage to be evaluated.

30

Claims

1. A fluidic analyser comprising a pre-concentrator, a fluid gating device and a detector, the fluid gating device being arranged to selectively route fluid from the pre-concentrator to either one of the detector and an exhaust port, characterised in that the pre-concentrator, fluid gating device and detector are each formed as substantially planar layers and arranged in a stack.
2. A fluidic analyser according to any preceding claim wherein the pre-concentrator comprises a layer of material having a plurality of apertures through which fluid can be passed, the internal surfaces of said apertures being adapted to releasably retain analytes from a fluid.
3. A fluidic analyser according to any preceding claim wherein the fluid gating device comprises a first outlet and a moveable member, the moveable member providing control over the flow of a received fluid to the first outlet, wherein the device is formed from a substantially planar substrate and in that the moveable member comprises a shutter that is moveable in the plane of the substrate
4. A fluidic analyser according to any preceding claim wherein the detector comprises a single electron transistor (SET) having a quantum dot region, wherein at least one molecule is attached to the SET in the vicinity of the quantum dot region and in that a receptor site for analytes is additionally provided adjacent said at least one molecule.
5. A fluidic analyser according to any one of the preceding claims and further comprising a pump.
6. A fluidic analyser as claimed in any preceding claim and further comprising a power source.

7. A pre-concentrator for releaseably retaining analytes from a fluid, characterised in that the pre-concentrator comprises a layer of material having a plurality of apertures through which fluid can be passed, the internal surfaces of said apertures being adapted to releaseably retain analytes from a fluid.
8. A pre-concentrator according to claim 7 wherein the internal surfaces defining said apertures are porosified.
9. A pre-concentrator according to any one of claims 7 to 8 wherein the substrate comprises a layer of silicon, said apertures being formed through said layer of silicon.
10. A pre-concentrator according to any one of claims 7 to 9 wherein said apertures are formed in the layer of material by deep reactive ion etching.
11. A pre-concentrator according to any one of claims 7 to 10 wherein the layer of material comprises a regular array of apertures.
12. A pre-concentrator according to claim 11 wherein the regular array of apertures is arranged to form a honeycomb structure.
13. A pre-concentrator according to any one of claims 7 to 12 wherein the internal surfaces of the apertures are reversibly adsorptive.
14. A pre-concentrator according to any one of claims 7 to 13 wherein said layer of material additionally comprises a heater element.
15. A pre-concentrator according to any one of claims 7 to 14 wherein said layer of material additionally comprises a heat sensor.
16. A pre-concentrator according to any one of claims 7 to 15 wherein said layer of material is mounted on a thermal isolation layer.

17. A pre-concentrator according to claim 16 wherein the thermal isolation layer comprises glass.

18. A fluidic device comprising a first outlet and a moveable member, the moveable member providing control over the flow of a received fluid to the first outlet, characterised in that the device is formed from a substantially planar substrate and in that the moveable member comprises a shutter that is moveable in the plane of the substrate.

19. A device according to claim 18 and further comprising an exhaust outlet for receiving any fluid that is prevented, by said moveable member, from passing to said first outlet.

20. A device according to any one of claims 18 to 19 wherein fluid is received by the device from a direction substantially perpendicular to the plane of the substrate.

21. A device according to any one of claims 18 to 20 wherein the entrance to the first outlet is defined in the planar substrate as a channel having an axis substantially perpendicular to the plane of the substrate.

22. A device according to any one of claims 18 to 21 wherein the shutter is shaped such that it can engage and seal the entrance to the channel defining the first outlet.

23. A device according to any one of claims 18 to 22 wherein the shutter can adopt either one of an open position and a closed position, the open position allowing fluid to pass to the first outlet and the closed position preventing fluid from passing to the first outlet.

24. A device according to claim 23 wherein, when the shutter is in the closed position, any received fluid is directed to an exhaust port.

25. A device according to claim 24 wherein, when the shutter is in the open position, fluid is prevented from flowing to the exhaust port.

26. A device according to any one of claims 23 to 25 wherein the moveable member comprises a means for retaining the shutter, without the application of power, in the open position or the closed position as required.
27. A device according to any one of claims 23 to 26 wherein the fluidic pathway through the device when the shutter is in the open position is minimised.
28. A device according to any one of claims 23 to 27 wherein the dead space of the device when the shutter is in the open position is minimised.
29. A device according to any one of claims 18 to 28 wherein the shutter is a micro-electromechanical (MEMS) shutter.
30. A device according to any one of claims 18 to 29 wherein the moveable member comprises a MEMS electro-thermal actuation mechanism to impart movement to the MEMS shutter.
31. A device according to claim 30 wherein the moveable member further comprises a MEMS compliant displacement mechanism.
32. A device according to any one of claims 18 to 31 wherein the planar substrate comprises silicon.
33. A device according to any one of claims 18 to 32 that is fabricated using a deep reactive ion etching process.
34. A gas flow controller comprises a device according to any one of claim 18 to 33.
35. A molecular detector comprising a single electron transistor (SET) having a quantum dot region, characterised in that at least one molecule is attached to the SET in

the vicinity of the quantum dot region and in that a receptor site for analytes is additionally provided adjacent said at least one molecule.

36. A detector according to claim 35 wherein said at least one molecule is a conjugated organic rod.

37. A detector according to any one of claims 35 to 36 wherein the at least one molecule is an organic molecule that comprises a side group to provide the receptor site.

38. A detector according to any one of claims 35 to 37 wherein a receptor site is provided on the substrate of the single electron transistor in the vicinity of said at least one molecule.

39. A device according to any one of claims 35 to 38 wherein a first end of the at least one molecule is attached to the source electrode of the single electron transistor and a second end of the at least one molecule is attached to the drain electrode of the single electron transistor.

40. A device according to claims 39 wherein the first and second ends of the at least one molecule are attached to the source and drain electrodes respectively via tunnel barriers.

41. A device according to any one of claims 35 to 40 wherein a self-assembled monolayer of molecules is located between the source and drain electrodes of the single electron transistor.

42. A device according to any one of claims 35 to 41 that additionally comprises means for measuring SET conductivity as a function of gate voltage.

43. A device according to any one of claims 35 to 42 that additionally comprises means for measuring SET conductivity as a function of source-drain voltage.

44. A device according to any one of claims 35 to 43 wherein the single electron transistor is formed from a complementary metal oxide semiconductor (CMOS) process .
45. A fluid analyser comprising a pre-concentrator according to any one of claims 7 to 17, a fluidic device according to any one of claims 18 to 34 and a detector according to any one of claims 35 to 44.
46. A fluid analyser as substantially hereinbefore described with reference to figures 1 to 11.
47. A pre-concentrator as substantially hereinbefore described with reference to figures 1 to 5.
48. A fluid gating device as substantially hereinbefore described with reference to figure 1 and figures 6 to 7.
49. A detector as substantially hereinbefore described with reference to figure 1 and figures 8 to 11.

AbstractFluid Analysis Apparatus

A fluid analyser (2) is described that comprises a pre-concentrator (4), a fluid gating device (6) and a detector (14). The fluid gating device (6) is arranged to selectively route fluid from the pre-concentrator (4) to either one of the detector (14) and an exhaust port (12). The pre-concentrator (4), fluid gating device (6) and detector (14) are each formed as substantially planar layers and arranged in a stack or cube.

Figure 1 refers

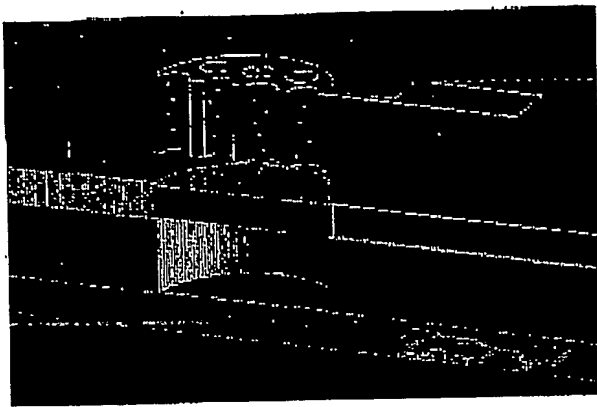


Fig 1a

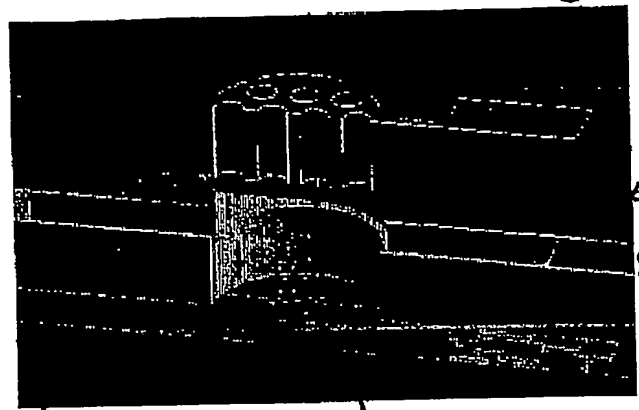


Fig 1b

FIGURE 1

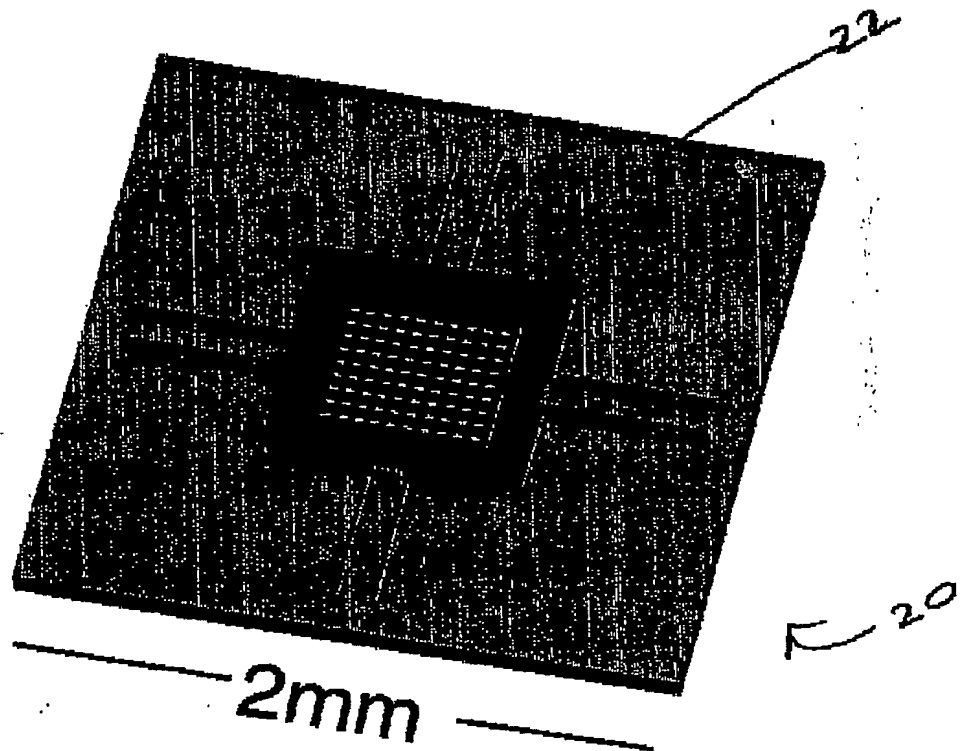


FIGURE 2

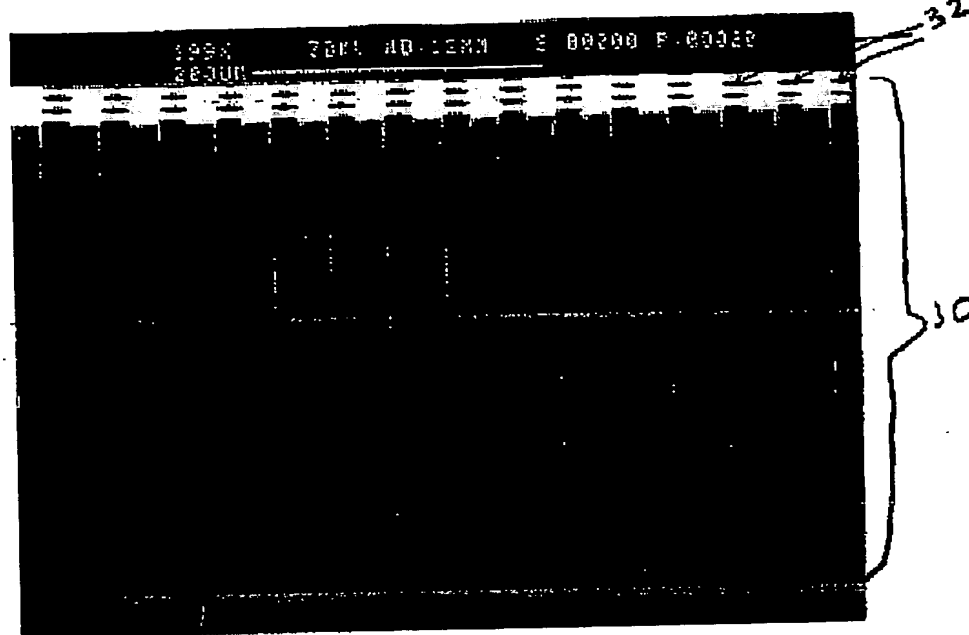


FIGURE 3

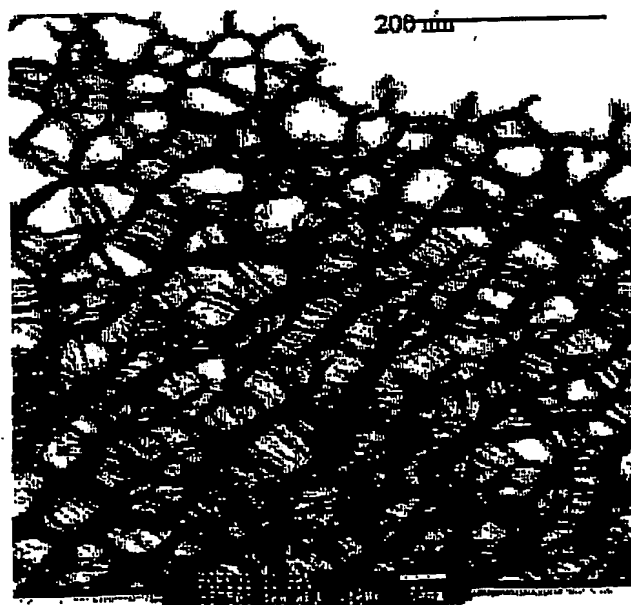


FIGURE 4

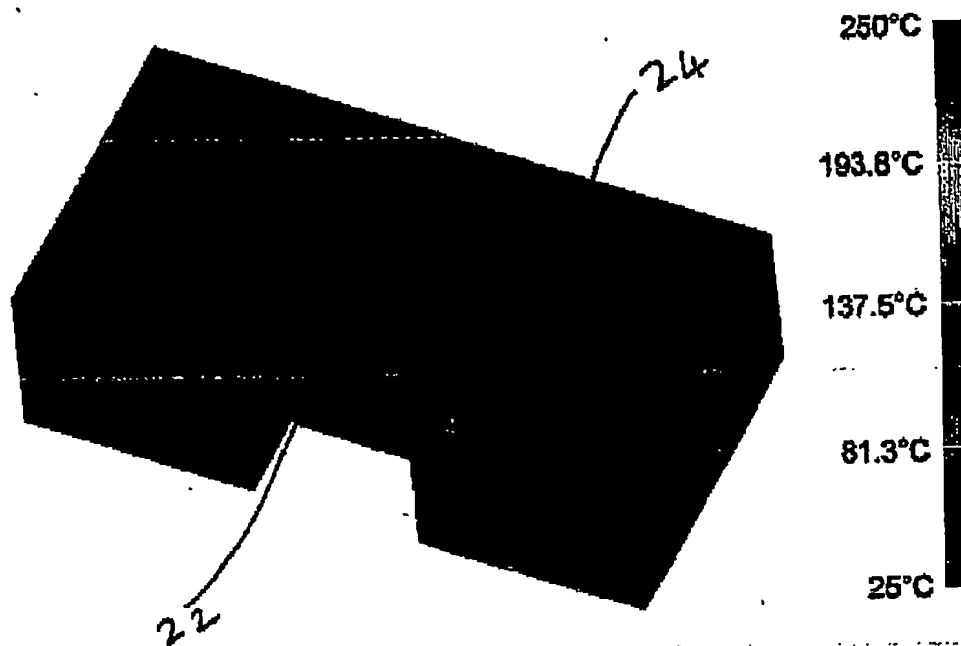


FIGURE 5

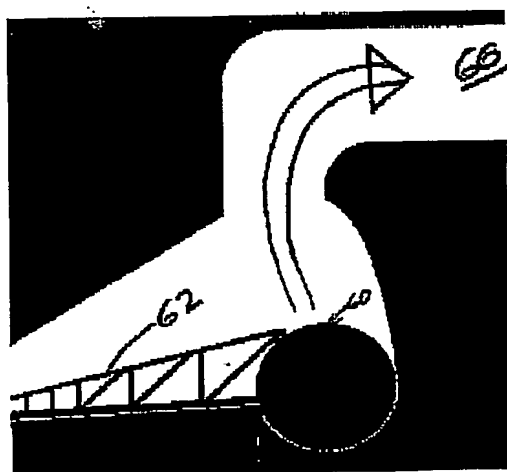


Fig 6a

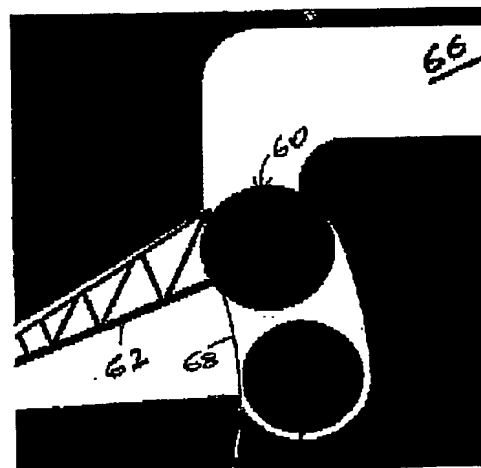


Fig 6b

FIGURE 6

3/6.

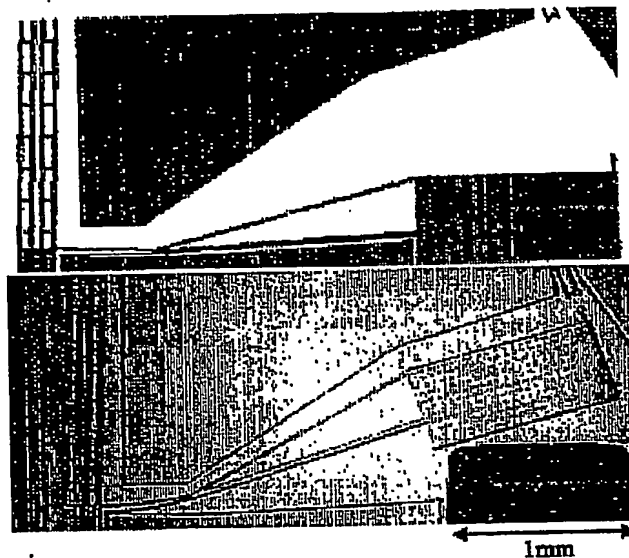


FIGURE 7

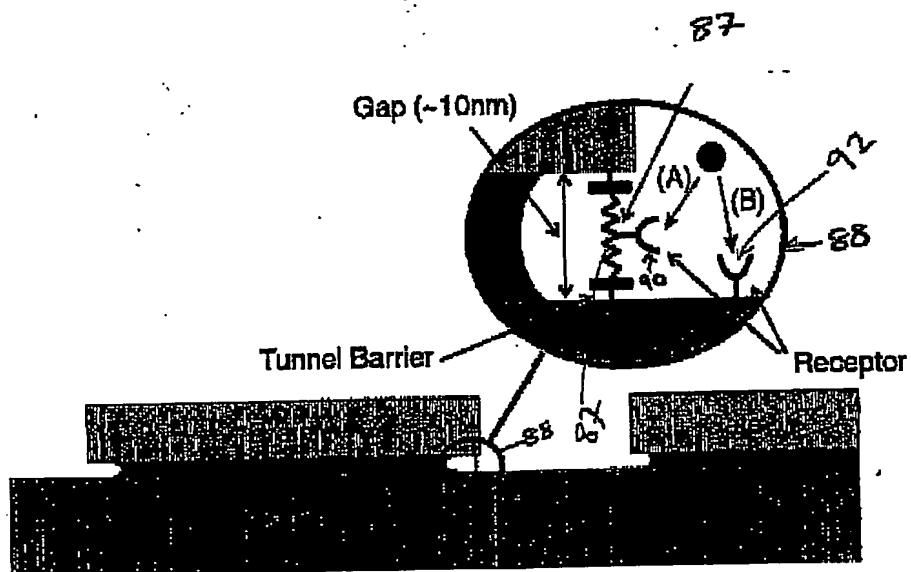


FIGURE 8

4/6

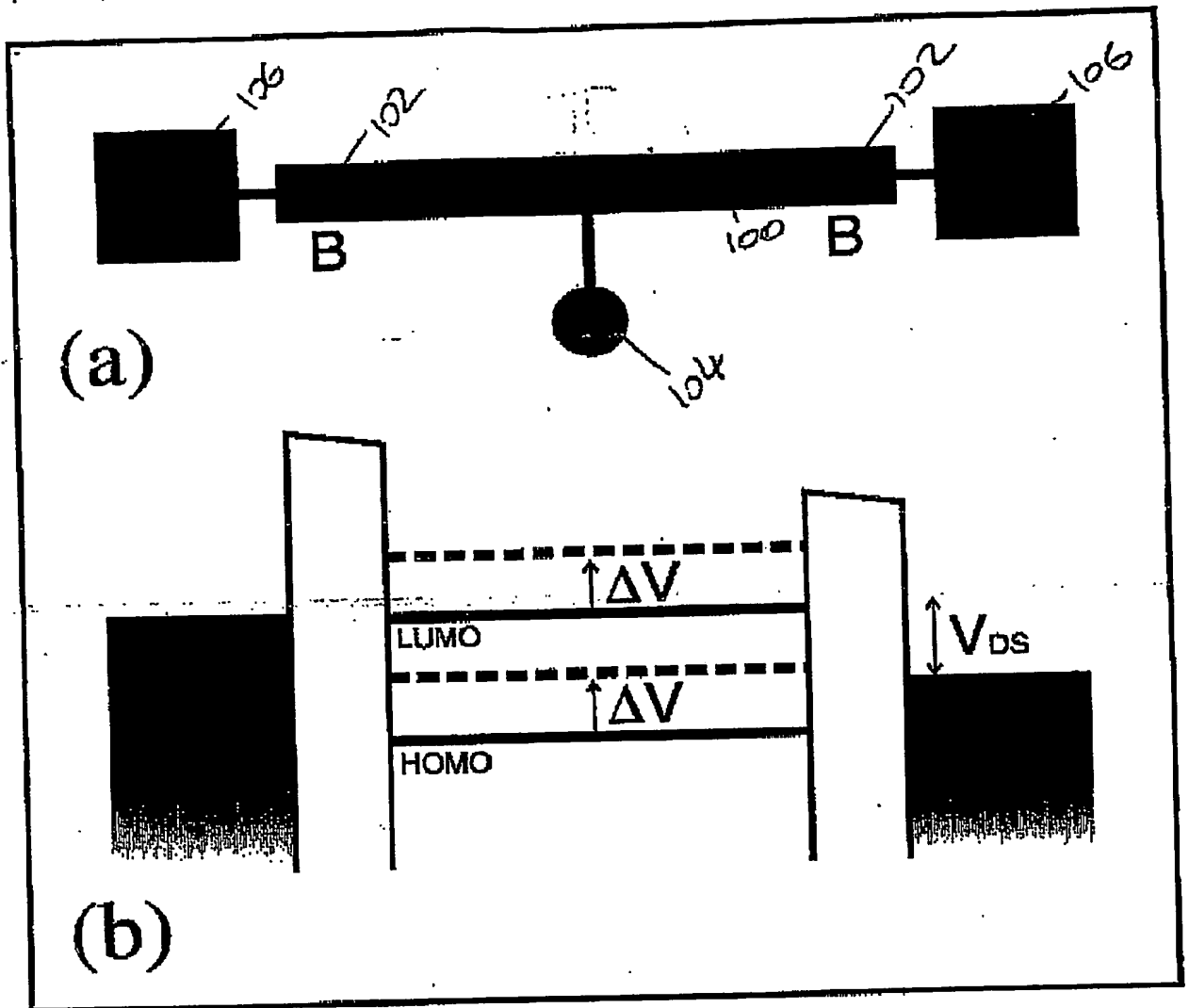


Figure 9

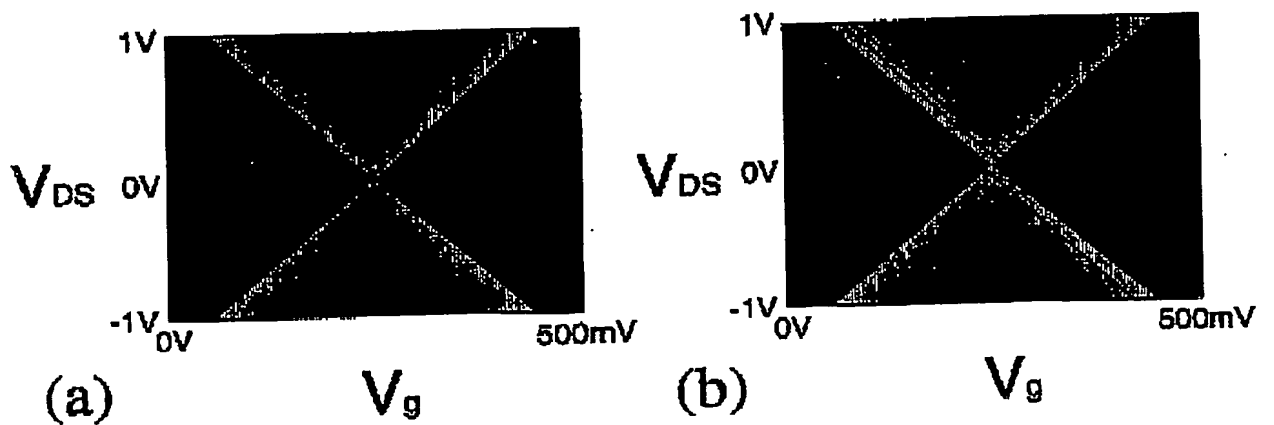
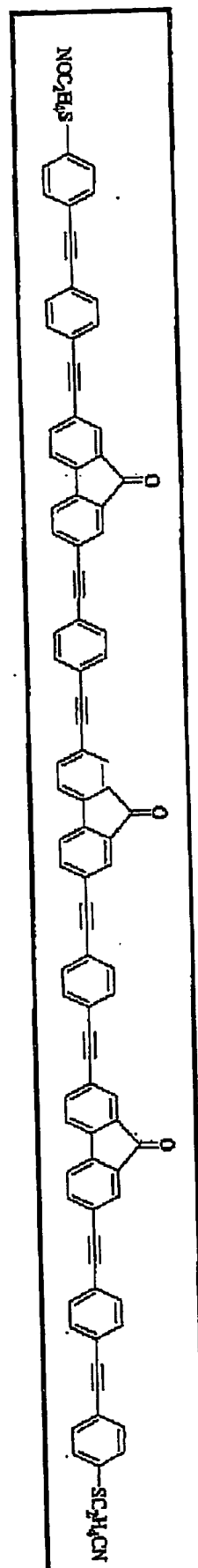


Figure 10

5/6

FIGURE 11



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